REMARKS

Claim 9 is now pending.

The Examiner has rejected claim 9 under 35 U.S.C. § 101 for allegedly lacking patentable utility and enablement. For reasons detailed below, the rejections should be withdrawn and claim 9 allowed to issue.

1. Claim 9 Has Patentable Utility

The Examiner has rejected claim 9 under 35 U.S.C. § 101 for allegedly lacking patentable utility. The Examiner states that:

> "No phenotype of the claimed transgenic mouse has been disclosed and the claimed transgenic mouse is indistinguishable from wild type mouse. Since the claimed transgenic mouse has no phenotype, one of ordinary skill in the art would not know where to look at the effect of an agent and how to determine if a pharmacological product is useful in medical application by using said transgenic mouse.... There is no correlation between a phenotype of the claimed transgenic mouse and a particular disease or disorder.... Basic research for studying the properties of a claimed product, a method of treating an unspecified disease or condition, and a method of assaying for or identifying a material that itself has "no specific and/or substantial utility" do not define "substantial utilities." Absent the phenotype of the claimed transgenic mouse and the correlation between a phenotype of said transgenic mouse and a particular disease or disorder, no "real world" use of the claimed transgenic mouse could be established."

The Examiner has further found the references cited by the Applicants to be unpersuasive.

Applicants disagree with the Examiner, and submit that disclosing a particular phenotype is not required to demonstrate a specific and substantial utility. The utility of these transgenic mice can be demonstrated by the numerous patents which have been issued to transgenic mice of this nature, which have been previously cited by Applicants. See U.S. Patent Nos. 5,922,927 ("the '927 patent"), 5,917,122 ("the '122 patent"), and 5,912,411 ("the '411 patent"), all of record. These patents are presumed to have specific and substantial utility, because issued patents, and each claim of an issued patent, are presumed to be valid. 35 U.S.C. §

282. Applicants note that the patents cited possess claims directed to transgenic mice which do not disclose specific phenotypes for the transgenic mice; in fact, the Examiner states that "no phenotype of the transgenic mouse in '927 has been disclosed." It follows that if the cited patents do not disclose a phenotype, but are otherwise presumed valid, then it is not necessary for a phenotype to be disclosed for a claim to be valid and to have a specific and substantial utility.

For example, claim 6 of the '927 patent is directed to a transgenic mouse comprising a Tn10-derived Tet repressor operably linked to a polypeptide which activates transcription in eukaryotic cells. As noted by the Examiner, this mouse would not display a phenotype distinct from a wild-type mouse of the same species. Like the present invention, the mouse of claim 6 of the '927 patent does not explicitly include any genes that would give rise to a phenotype that would provide a "correlation between a phenotype of the claimed transgenic mouse and a particular disease or disorder." Similar claims can be found in claim 6 of the '122 patent and claim 1 of the '411 patent. Accordingly, Applicants submit that the presence of a phenotype which is distinct from the phenotype of a wild-type animal is not required to show utility, otherwise these claims would not have issued in the cited patents. Accordingly, it is not necessary for the mouse of claim 9 to express a phenotype distinct from the wild-type phenotype in order to show a specific and substantial utility.

In addition, a person of ordinary skill in the art would understand that a phenotype distinct from a wild-type mouse is neither necessary nor desirable for the transgenic mouse to be useful. As argued in the prior amendment, the utility of the present invention lies in the consistent expression of the reverse tetracycline controlled activator in the tissues of the transgenic animal, resulting from the promoter activity of the EF-1α promoter. A second gene of interest to be studied is also inserted, which may be activated based upon the presence of

tetracycline. See, e.g., specification at page 1, line 6 to page 2, line 29, and at page 21, lines 27-32. By selectively activating the gene of interest, comparisons between the phenotypes of the activated and unactivated transgenic mice can be made. *Id.* Absent activation of the second gene of interest, it would not be desirable for the transgenic mouse to display an overt non-wildtype phenotype, which would detract from its value as a model system and interfere with the study of the second gene of interest. The fact that the claimed transgenic mouse displays no phenotype makes it more useful, not less; it effectively allows comparison of an overt phenotype (activated transgenic mouse) with a wildtype phenotype (unactivated transgenic mouse). This comparison also serves as an additional control, as it eliminates the possibility that insertion of the transgene itself is causing the phenotype. Accordingly, based upon the disclosure in the specification, a person of ordinary skill in the art would understand that the claimed transgenic mouse is useful for the study of genes, because it allows for the controlled study of a gene of interest.

The fact that the phenotype of the transgenic mouse varies with the second gene of interest also does not detract from the substantial utility of the invention. Applicants need only show that there is a reasonable correlation between the activity in question and the asserted utility. See MPEP § 2107.02 ("[T]he applicant does not have to provide evidence sufficient to establish that an asserted utility is true 'beyond a reasonable doubt....' Nor must an applicant provide evidence such that it establishes an asserted utility as a matter of statistical certainty.... Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true.") (emphasis in original). Applicants have shown that the transgenic mouse of the present invention can be used to effect the controlled expression of a gene of interest in the mouse. It is not relevant that the level of

expression of the gene of interest and the phenotype induced may vary; because a person of ordinary skill in the art would appreciate that it is more likely than not true that the transgenic mouse could be used to selectively activate a gene of interest. As noted above, the ability to selectively activate a gene of interest, regardless of the resulting phenotype, is widely recognized by persons of ordinary skill in the art as a powerful and useful research tool. See Chin *et al.*, TIG (2000) 16(4):147-150, 147, already of record (stating that conditional transgene expression systems, such as the Tet system, "provide a means to assess the physiological roles of oncogenes in tumorigenesis and to determine the consequences of their remediation.").[1]

The Examiner is erroneously equating usefulness for performing research with the need to perform research to confirm utility. While the primary use of the transgenic mouse of the present invention may be in the field of research, the transgenic mouse of the present invention does not require further research to confirm its utility. The fact that the utility of the present invention lies primarily in research does not detract from its "real world" utility. See MPEP § 2107.01 ("Many research tools... have a clear, specific, and unquestionable utility.... An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact 'useful' in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm."). Transgenic mice such as the one claimed in the present invention have a well-known utility, and are useful for performing research. See Chin, supra; see also U.S. Patent Nos. 5,922,927,

[1] Applicants also note that it is not required that all utilities be proven. See MPEP § 2107.02 ("[A]n applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility."). Accordingly, the present invention still possesses substantial utility even if its utility is limited only to the study of oncogenes and tumorigenesis.

5,917,122, and 5,912,411. The utility of the mouse does not lie solely in the EP-1α promoter and reverse tetracycline transactivator protein alone; the utility lies in the ability to insert a gene of interest into the mouse, and to control its expression via the EP-1α promoter and reverse tetracycline transactivator protein. The fact that the phenotype of the mouse changes depending upon the second gene of interest adds to the utility of the mouse, and demonstrates its versatility as a research tool. See specification at page 2, lines 26-29 (the tetracycline inducible system's "versatility has enabled adaption to situations requiring inducible expression in a tissue specific or generalized manner in animal or plant models, opening new avenues to study gene function in vivo.").

Based upon the foregoing arguments, Applicants submit that the present specification and state of the art at the time of filing provide more than adequate evidence to prove substantial utility for the present invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

2. Claim 9 is Enabled

The Examiner has rejected claim 9 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner cites the reasons set forth in the prior Office Action, where the Examiner stated:

> "The specification fails to provide adequate guidance and evidence for the production of numerous heterozygous or homozygous transgenic non-human animals, which have their phenotypes that are distinguishable from corresponding wild-type animals.... In view of the inherent unpredictability of the resulting phenotypes of the claimed transgenic animals, the lack of evidence for the phenotypes of the claimed transgenic non-human animals, and the limitations of the use of ES cells for generating transgenic animals, one skilled in the art at the time of the invention would not know how to use the claimed transgenic non-human animals with unknown phenotypes."

The Examiner also cites the arguments set forth above regarding the rejection under 35 U.S.C. § 101.

Applicants submit that, based on the foregoing arguments, the Examiner's rejection under 35 U.S.C. § 101 has been obviated. See MPEP § 2164.07(II). As noted above, several patents have issued claiming transgenic mice similar to the one claimed in the present invention, which are not disclosed to have phenotypes which are different from wild-type mice of the same species. Because these patents are presumed to be valid, it must be presumed that they provide an enabling disclosure on how to make and use the transgenic mice. Accordingly, it is not necessary to disclose a distinct phenotype in order to provide an enabling disclosure.

Furthermore, the Examiner is erroneously and improperly looking beyond the claimed invention, which is directed to a transgenic mouse comprising the EP-1α promoter operably linked to a reverse tetracycline controlled transactivator protein. See MPEP § 2164.08 ("All questions of enablement are evaluated against the claimed subject matter."). The possibility that the phenotype may vary, based upon the identity of the second gene of interest, does not make mean that the skilled artisan would not understand, based upon the specification, "how to use" the claimed invention.. Relying on the disclosure of the instant specification, a person of ordinary skill in the art could predictably generate a transgenic mouse in which the expression of a second gene of interest could be controlled, irregardless of the resulting phenotype of that mouse. Applicants have provided detailed and clear methods on how to generate the transgenic expression cassette. See specification at page 12-17, 22. Applicants have also clearly disclosed methods for making and using transgenic mice as claimed. See specification at pages 20-21. Furthermore, the generation of transgenic mice is well-known in the art, and it would take a person of ordinary skill in the art no more than routine

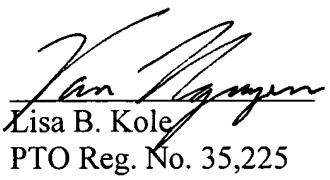
experimentation to make and use the transgenic mice of the present invention. Thus, the specification provides more than adequate information to enable a person of ordinary skill in the art to practice the present invention.

Accordingly, Applicants submit that the present invention is enabled by the specification as of the time of filing, and respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Entry of the foregoing remarks into the file of the above-identified application is respectfully requested. The Applicant believes that the invention described and defined by claim 9 are patentable over the rejections of the Examiner. Withdrawal of the rejections and reconsideration of the claims is requested. An early allowance is earnestly sought.

Respectfully submitted,



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